Claim 45 was added to recite a molecular weight of between "120 and 156 kD." This amendment adds no new matter. Support for this amendment can be found, e.g., in claim 1 as originally filed.

Claim 46 was amended to recite a "homomeric potassium channel." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 15, lines 21-22.

Claim 47 was amended to recite a "heteromeric potassium channel." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 15, lines 22-23.

Claim 48 was amended to recite hybridization conditions that end with a wash step "at 65°C in a solution comprising 0.2x SSC and 0.1% SDS." This amendment adds no new matter. Support for this amendment can be found, e.g., in the specification on page 24, lines 10-11.

35 U.S.C. § 112, second paragraph

"Molecular weight"

Claims 1 and 13 have been rejected as allegedly indefinite for reciting the molecular weight values To expedite prosecution, claims 1 and 13 have been amended to delete the molecular weight values. Applicants therefore respectfully request that the rejection be withdrawn for the purposes of claims 1 and 13.

New dependent claim 45 recites a molecular weight range. With respect to claim 14, Applicants respectfully traverse the rejection. In the context of molecular weight determination, one of skill in the art would understand that the values could be obtained using standard methods such as SDS-PAGE or chromatography using standard molecular weight markers. Furthermore, in the present specification, Applicants reference standard molecular biology texts such as Sambrook and Ausubel, which described such methodologies (*see, e.g.,* specification page 29, lines 3-6). The specification and claims therefore meet the threshold

clarity and precision standards of the statute. MPEP § 2173.02. As described by the court in *In re Chilowsky*,

> It is well settled that the disclosure of an application embraces not only what is expressly set forth in words or drawings, but what would be understood by persons skilled in the art. . . . That which is common and well known is as if it were written out in the patent. *In re Chilowsky*, 108 USPQ 321, 324 (C.C.P.A. 1956).

Applicants therefore respectfully request that the rejection be withdrawn.

"SEQ ID NO:"

Claims 1, 7, 17, and 26 were rejected because the recited sequences are "mere characters on a page.' To expedite prosecution, the claims have been amended to recite polypeptides and nucleotides comprising a particular SEQ ID NO:. Applicants therefore respectfully request that the rejection be withdrawn.

"mSlo3" and "hSlo3"

Claims 2 and 3 were rejected as allegedly indefinite for reciting mSlo3 and hSlo3 polypeptides. Applicants respectfully traverse, and point out that these terms are defined in the specification on page 13, line 31 to page 14, line 3 and page 14, lines 16-25. Applicants respectfully request that the rejection be withdrawn.

"Moderately stringent hybridization conditions"

Claims 6-7 and 13 have been rejected as allegedly indefinite for reciting the phrase "moderately stringent hybridization conditions." To expedite prosecution, the claims have been amended to recite moderately stringent hybridization conditions, as defined in the specification. Applicants therefore respectfully request that the rejection be withdrawn.

"Stringent hybridization conditions"

Claims 10-11 have been rejected as allegedly indefinite for reciting the phrase "stringent hybridization conditions." Applicants respectfully traverse the rejection. In the context of PCR reactions, one of skill in the art would understand the phrase "stringent hybridization conditions" as referring to standard conditions for such reactions, thereby meeting the threshold clarity and precision standards of the statute. MPEP § 2173.02. As described by the court in *In re Chilowsky*,

> It is well settled that the disclosure of an application embraces not only what is expressly set forth in words or drawings, but what would be understood by persons skilled in the art. . . . That which is common and well known is as if it were written out in the patent. *In re Chilowsky*, 108 USPQ 321, 324 (C.C.P.A. 1956).

The present application discloses to the use of primers to amplify nucleic acids. The present application further discloses prior art materials that teach standard conditions for reactions using degenerate primers (*see, e.g.*, specification page 31, lines 8-9, referring, e.g., to *PCR Protocols: A Guide to Methods and Applications*, (Innis *et al.*, eds., 1990)). One of skill in the art would therefore clearly understand that phrase "stringent conditions," as used in the context of PCR reactions, refers to standard conditions known to those of skill in the art. Applicants therefore respectfully request that the rejection be withdrawn.

"Variant"

Claim 12 has been rejected as allegedly indefinite for reciting the term "variant." To expedite prosecution, the claim has been amended to delete this term. Applicants therefore respectfully request that the rejection be withdrawn.

"Core domain"

Claim 14 has been rejected as allegedly indefinite for reciting the phrase "core domain." To expedite prosecution, the claims have been amended to recite that the core domain

is amino acids 35-641 of SEQ ID NO:1. Applicants therefore respectfully request that the rejection be withdrawn.

35 U.S.C. § 112, first paragraph

"Unspecified hybridization conditions"

Claims 6-7, 10-11, and 13 were rejected as allegedly lacking enablement for hybridization under "unspecified hybridization conditions." Applicants first point out that the claims have been amended to recite hybridization conditions. Furthermore, as described above, for PCR reactions, such conditions are well known in the art and are described in the specification. To the extent that the rejection still applies to the claims as amended, Applicants respectfully traverse. Applicants have clearly defined moderate and highly stringent hybridization conditions in the specification on page 24, lines 8-16. Applicants therefore respectfully request that the rejection be withdrawn.

"Variants"

Claim 12 was rejected as allegedly lacking enablement for reciting "variants thereof." To expedite prosecution, Applicants have amended the claims to delete this term. However, this term is clearly defined in the specification on page 17, line 20 to page 18, line 6. Applicants therefore respectfully request that the rejection be withdrawn.

"60% identity to a core domain"

Claim 14 was rejected for allegedly lacking enablement for reciting a nucleic acid encoding a polypeptide having a core domain with at least 60% identity to a Slo3 core domain. Applicants first note that to expedite prosecution, the claims have been amended to recite that the core domain is amino acids 35 to 641 of SEQ ID NO:1. To the extent that the rejection applies to the claims as amended, Applicants respectfully traverse the rejection. The claims recite both functional and structural elements that allow the routine identification of Slo nucleic acids and proteins, using the assays provided in the specification. Moreover, Applicants clearly meet the

PTO guidelines for enablement, which set forth the standard for the scope of enablement when a large number of possible embodiments exists.

a. Identification of functional Slo3 proteins does not require undue experimentation

The rejection alleges that the specification provides enablement only for identifying nucleic acids encoding a Slo3 protein of SEQ ID NO:1, 3, 16, or 18. However, the claims have been amended to recite functional and structural characteristics of the claimed family of Slo3 proteins. The present application also provides working examples and functional assays for identification of nucleic acids encoding the claimed family of Slo3 proteins, without undue experimentation. The assays and examples of the specification, together with standard methodology known to those of skill in the art, therefore provide adequate guidance for identifying nucleic acids encoding the Slo3 proteins of the invention.

As identified by the Patent Office and the Federal Circuit, whether undue experimentation is required by one skilled in the art to practice the invention is determined by considering factors such as the amount of guidance presented in the application and the presence of working examples. *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int. 1985); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). As described in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should precede." *Wands*, 8 USPQ2d at 1404 (quoting *In re Jackson*, 217 USPQ 804 (Bd. Pat. App. & Int. 1982).

The present invention describes a family of nucleic acids encoding Slo3 proteins which functionally: (1) have a unit conductance of approximately 80-120 pS when the monomer is in a functional tetrameric form of a potassium channel and is expressed in a *Xenopus* oocyte; and (2) have increased activity above approximately intracellular pH of 7.1; and which structurally either: (1) hybridize to reference Slo3 nucleic acids; (2) are amplified by primers that hybridize to the reference Slo3 nucleic acids; (3) have greater than about 60% homology to a

reference Slo3 core domain; or (4) bind to polyclonal antibodies raised against reference Slo3 polypeptides.

At the time of the present invention, identification of nucleic acids having the functional and structural characteristics described above was well within the means of one of skill of the art, without undue experimentation. Standard hybridization, PCR, and sequence alignment techniques were available, as well as the PCR, hybridization, sequence alignment, and functional assays disclosed in the specification. For example, one of skill in the art could use standard hybridization and PCR assays to identify nucleic acids encoding the Slo3 of the invention (*see, e.g.*, specification, page 28, line 25 to page 32, line 10). Furthermore, one of skill in the art could use manual or computer sequence alignment to determine whether potential Slo3 sequences have the specified homology (*see, e.g.*, page 19, line 30 to page 23, line 2).

Finally, numerous functional assays to identify Slo3 polypeptides were known to those of skill in the art. For example, the specification describes *Xenopus* oocyte expression to determine the characteristic of unit conductance of approximately 80-120 pS when the monomer is in a functional tetrameric form of a potassium channel and is expressed in a *Xenopus* oocyte; and the characteristic of increased activity above approximately intracellular pH of 7.1; (see, e.g., Example III). The assays described in the specification, coupled with methodology well known to those of skill in the art, therefore demonstrate that screening for nucleic acids encoding Slo3 proteins having the structural and functional characteristics described above is routine.

The specification thus provides a number of different assays and working examples, demonstrating that any experimentation that may be required to identify functional Slo3 proteins of the invention is not undue. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants therefore respectfully request that the rejection be withdrawn.

B. One of skill could readily determine any one of the claimed embodiments

Furthermore, regarding the issue of enablement for nucleic acids, where a large number of possible embodiments exists, the PTO has provided express guidelines for examination. As set forth in the MPEP at § 2168.08, a rejection of claims such as those in the

present application for undue breadth is inappropriate where "one of skill could readily determine any one of the claimed embodiments."

This standard is further explained in the "Training Materials for Examining Patent Applications with Respect to 35 U.S.C. § 112, First Paragraph--Enablement Chemical/Biotechnological Applications," section III.A.2.b.i.(c). In the Guidelines, the PTO specifically answers the question regarding scope of a nucleic acid composition claim (e.g., as applied to the present case, nucleic acid encoding a Slo3 polypeptide) left unanswered by the Federal Circuit in *In re Deuel*, 34 USPQ2d 1210, 1216 (Fed. Cir. 1995). The claims at issue in *Deuel* were directed to any DNA encoding a specific amino acid sequence. Thus, a very great number of nucleic acid molecules were within the scope of the claims. In fact, the number was so great that a listing of all possible DNAs encoding the protein was a practical impossibility.

In the Guidelines, the PTO addresses this issue, explaining that "even though a listing of all the possible DNAs which encode a given protein is a practical impossibility due to the enormous number of such nucleic acids, any particular sequence can be written by one of skill given the disclosure and the sequence can be ordered from a company which synthesizes DNA." In this manner, one of skill in the art can readily determine any one of the embodiments. The PTO concluded that scope rejections such as the one hypothesized in *Deuel* should not be advanced.

In the present application, one of skill in the art has only to identify an Slo3 polypeptide nucleic acid which either: (1) hybridizes to reference Slo3 nucleic acids; (2) is amplified by primers that hybridize to the reference Slo3 nucleic acids; (3) has greater than about 60% homology to a reference Slo3 core domain; or (4) binds to polyclonal antibodies raised against reference Slo3 polypeptides, using techniques described in the specification and known to those of skill in the art. Such an Slo3 encoding nucleic acid is then tested, using the routine assays described in the specification, for the prescribed functionality. Although many Slo3 encoding nucleic acid sequences are theoretically possible, one of skill can readily determine, one by one, any particular Slo3 encoding sequence, without undue experimentation. Thus, in the present application the skilled artisan can readily, with only routine experimentation, make and

test any particular Slo3 encoding nucleic acid. Applicants therefore respectfully request that the rejection be withdrawn.

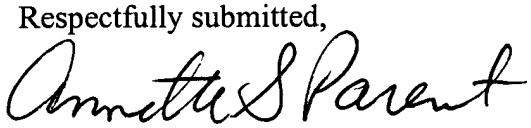
35 U.S.C. § 102

Claim 12 was rejected as allegedly anticipated by McCobb *et al.* To expedite prosecution, claim 12 has been amended to recite a nucleic acid encoding at least 25 contiguous amino acids from a pH sensitive potassium channel. Applicants therefore respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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